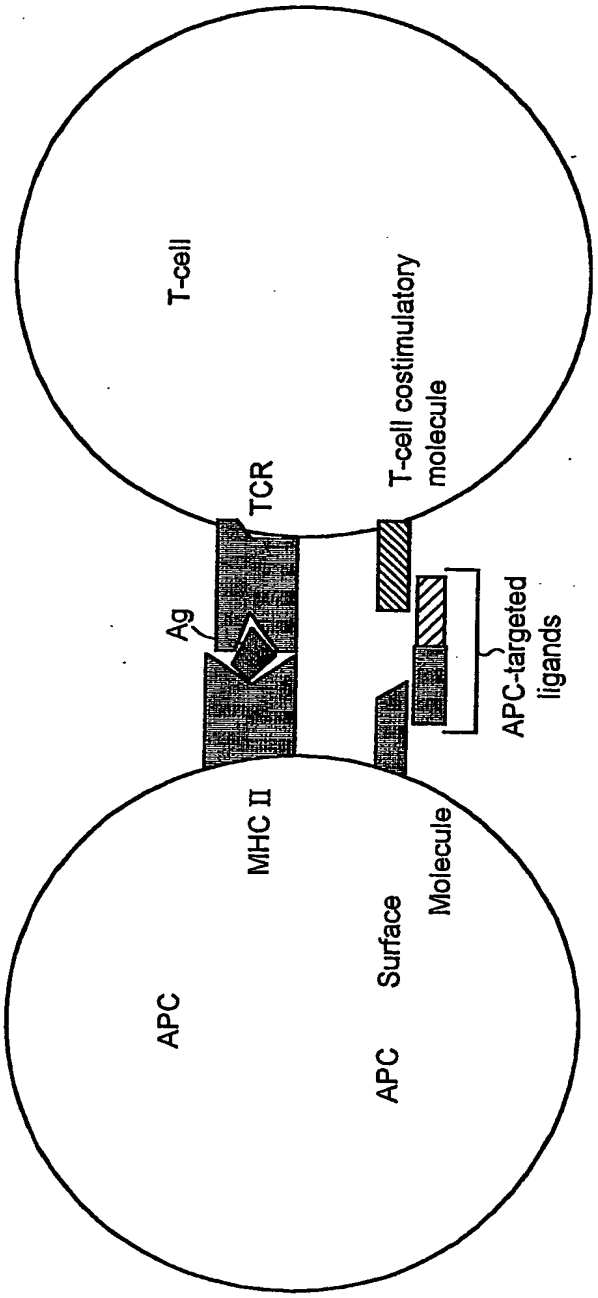

T-cell
T-cell costimulatory molecule
TCR
Ag
APC-targeted ligands
MHC II
Molecule
Surface
APC
APC

FIG. 1

FIGURE 2

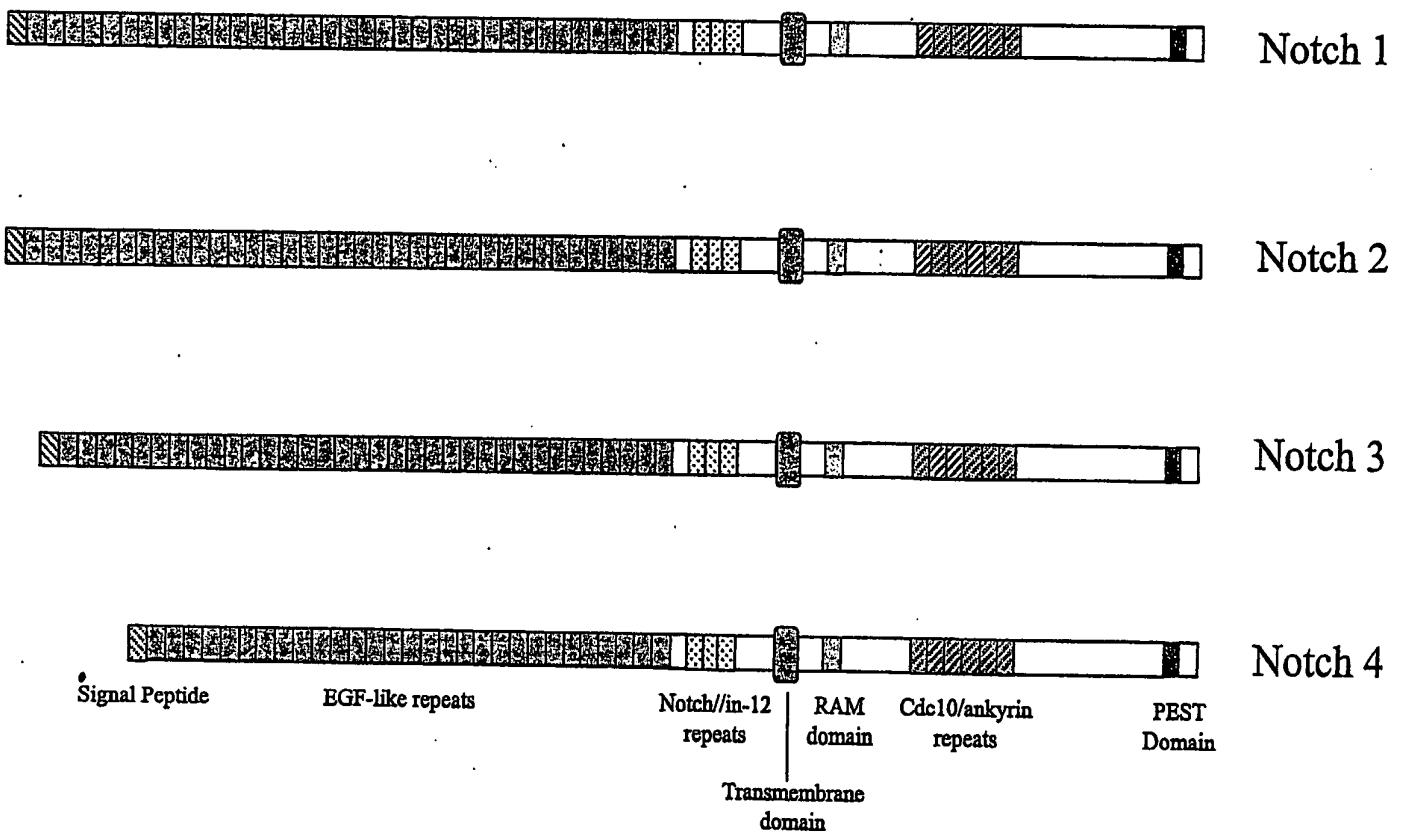

Notch 1
Notch 2
Notch 3
Notch 4
Signal Peptide
EGF-like repeats
Notch//in-12 repeats
RAM domain
Cdc10/ankyrin repeats
PEST Domain
Transmembrane domain

FIGURE 3

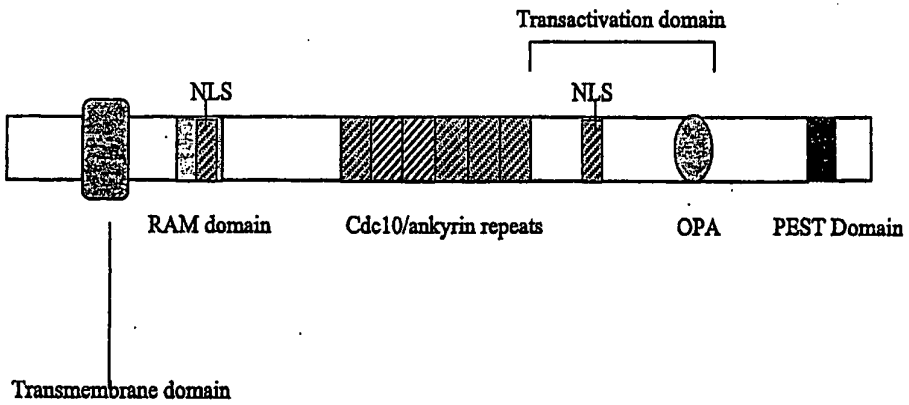
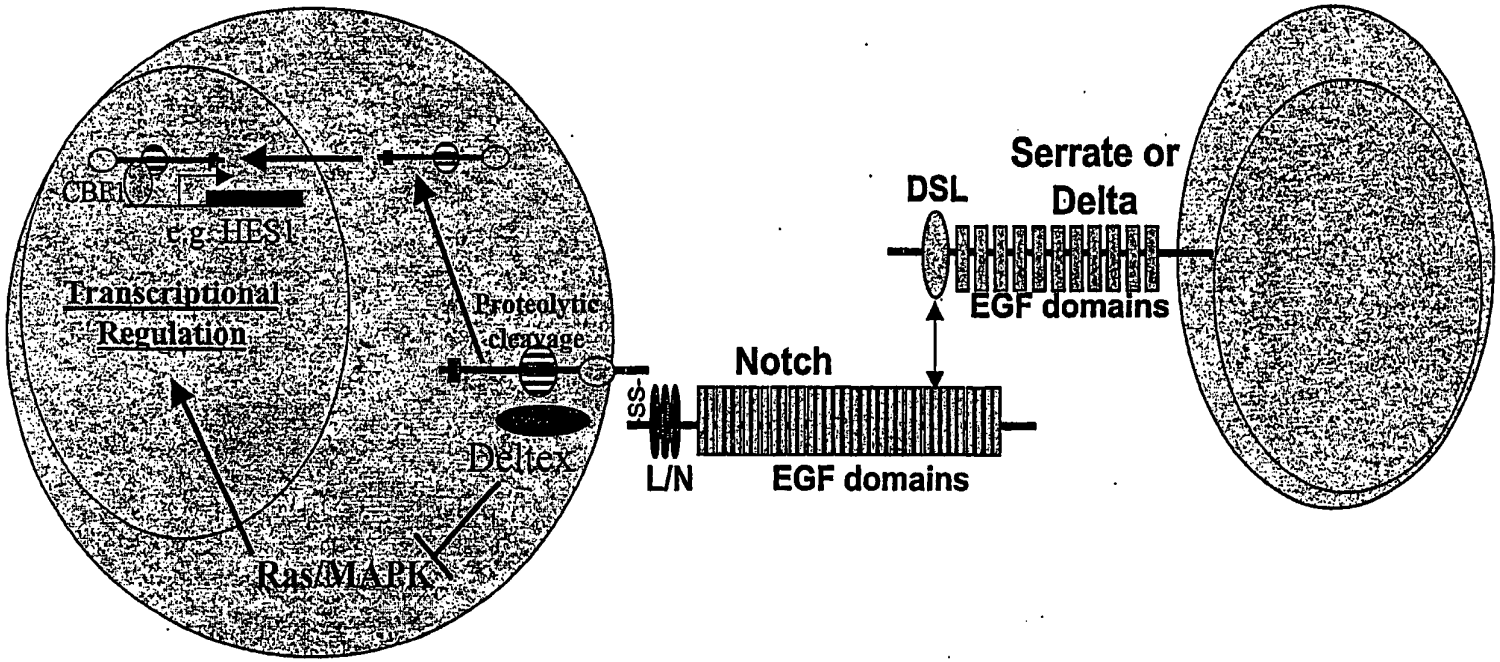

Transactivation domain
NLS
NLS
RAM domain
Cdc10/ankyrin repeats
OPA
PEST Domain
Transmembrane domain

Figure 4


CBF1
e.g. HES1
Transcriptional Regulation
Proteolytic cleavage
Deltex
Ras/MAPK
SS-
L/N
Notch
EGF domains
DSL
Serrate or Delta
EGF domains

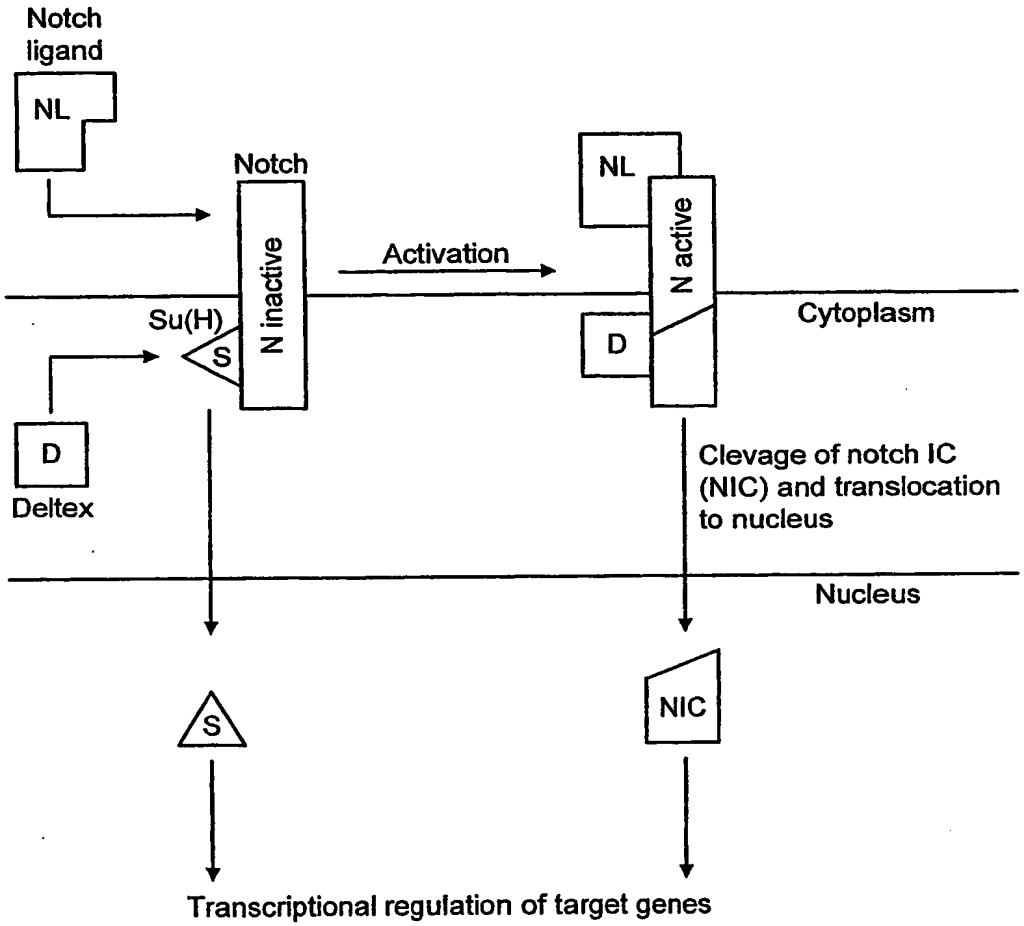

Notch
ligand
NL
Notch
N inactive
Activation
NL
N active
Cytoplasm
Su(H)
S
D
D
Deltex
Clevage of notch IC
(NIC) and translocation
to nucleus
Nucleus
S
NIC
Transcriptional regulation of target genes

FIG. 5

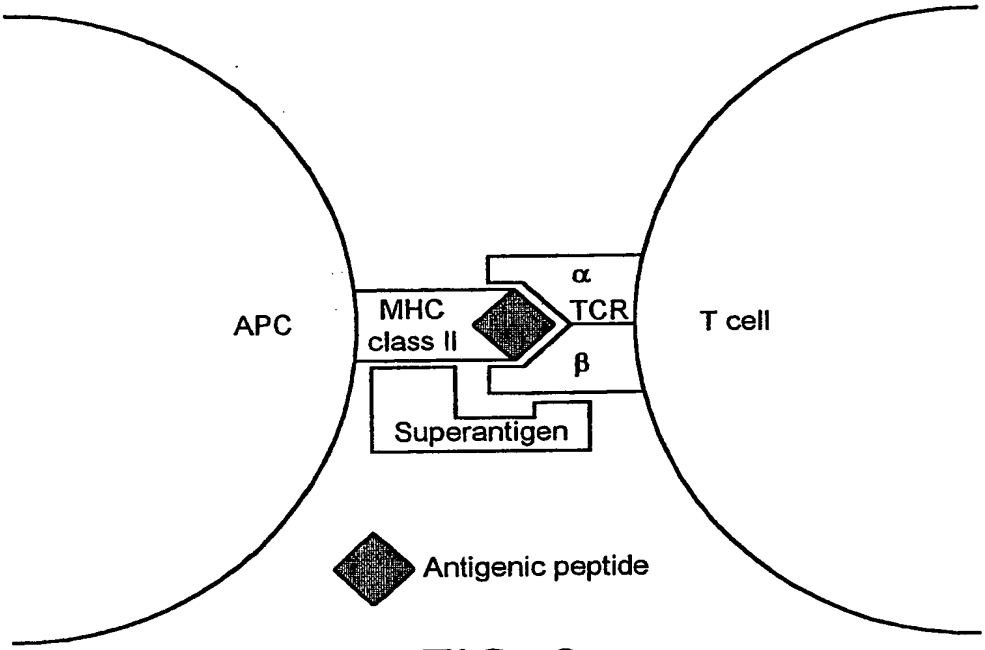

APC
MHC
class II
α
TCR
β
T cell
Superantigen
Antigenic peptide

FIG. 6

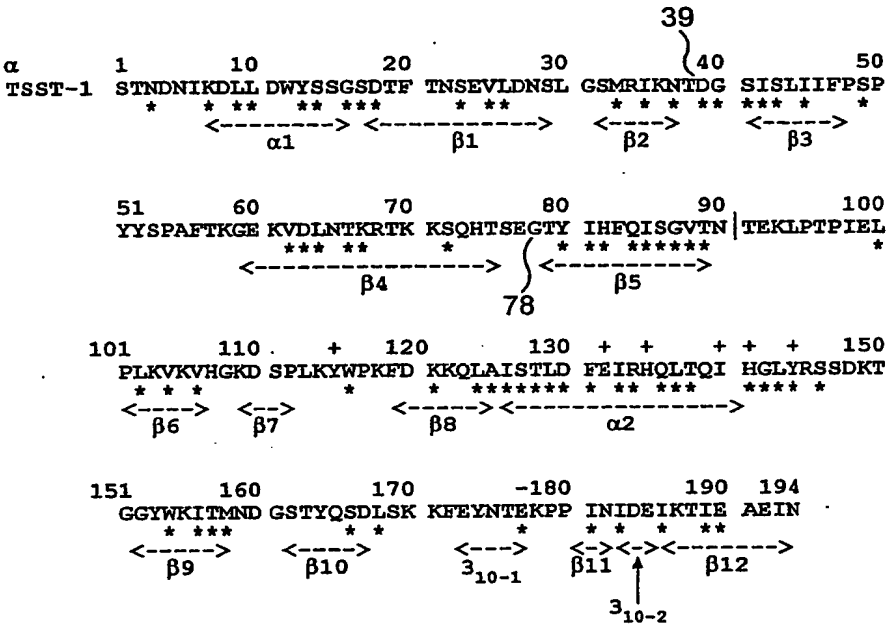

39
α 1 10 20 30 40 50
TSST-1 STNDNIKDLL DWYSSGSDTF TNSEVLDNSL GSMRIKNTDG SISLIIFPSP
α1 β1 β2 β3
51 60 70 80 90 100
YYSPAFTKGE KVDLNTKRTK KSQHTSEGTY IHFQISGVTN TEKLPTPIEL
β4 β5
78
101 110 120 130 150
PLKVKVHGKD SPLKYWPKFD KKQLAISTLD FEIRHQLTQI HGLYRSSDKT
β6 β7 β8 α2
151 160 170 180 190 194
GGYWKITMND GSTYQSDLSK KFEYNTEKPP INIDEIKTIE AEIN
β9 β10 3 10-1 β11 β12
3 10-2

FIG. 7


Trans-membrane region
Signal peptide
DSL domain
EGF repeats
Cysteine-rich region
Jagged
Delta

Figure 8

```
DL_DROME/164-226      WKTNKSESQ.....YT----SLEYDFRVTCDLNYYGSGCAKFCRPRDDSFGHSTCSETGEIICLTGWQGDYC
DLL1_HUMAN/159-221    WSQDLHSSG.....RT----DLKYSYRFVCDEHYYGEGCSVFCRPRDDAFGHFTCGERGEKVCNPGWKGPYC
DLL1_MOUSE/158-220    WSQDLHSSG.....RT----DLRYSYRFVCDEHYYGEGCSVFCRPRDDAFGHFTCGDRGEKMCDPGWKGQYC
DLL1_RAT/158-220      WSQDLHSSG.....RT----DLRYSYRFVCDEHYYGEGCSVFCRPRDDAFGHFTCGERGEKMCDPGWKGQYC
DLL4_MOUSE/156-218    WRTDEQNDT.....LT----RLSYSYRVICSDNYYGESCSRLCKKRDDHFGHYECQPDGSLSCLPGWTGKYC
DLL4_HUMAN/155-217    WLLDEQTST.....LT----RLRYSYRVICSDNYYGDNCSRLCKKRNDHFGHYVCQPDGNLSCLPGWTGEYC
Rat J1(Q63722)        WQTLKQNTG.....IA----HFEYQIRVTCDDHYYGFGCNKFCRPRDDFFGHYACDQNGNKTCMEGWMGPEC
Mouse J1(Q9QXX0)      WQTLKQNTG.....IA----HFEYQIRVTCDDHYYGFGCNKFCRPRDDFFGHYACDQNGNKTCMEGWMGPDC
Human J1 (O15122)     WQTLKQNTG.....VA----HFEYQIRVTCDDYYYGFGCNKFCRPRDDFFGHYACDQNGNKTCMEGWMGREC
Chick J1 (Q90819)     WQTLKHNTG.....AA----HFEYQIRVTCAEHYYGFGCNKFCRPRDDFFTHHTCDQNGNKTCLEGWTGPEC
Chick J2 (O42347)     WKTLQFNGP.....VA----NFEVQIRVKCDENYYSALCNKFCGPRDDFVGHYTCDQNGNKACMEGWMGEEC
Mouse J2 (Q9QYE5)     WKSLHFSGH.....VA----HLELQIRVRCDENYYSATCNKFCRPRNDFFGHYTCDQYGNKACMDGWMGKEC
Human J2 (Q9UNK8)     WKSLHFSGH.....VA----HLELQIRVRCDENYYSATCNKFCRPRNDFFGHYTCDQYGNKACMDGWMGKEC
Rat J2 (P97607)       WKSLHFSGH.....VA----HLELQIRVRCDENYYSATCNKFCRPRNDFFGHYTCDQYGNKACMDGWMGKEC
Human J2 (Q9Y219)     WKSLHFSGH.....VA----HLELQIRVRCDENYYSATCNKFCRPRNDFFGHYTCDQYGNKACMDGWMGKEC
SERR_DROME/221-283    WKTLDHIGR.....NA----RITYRVRVQCAVTYYNTTCTTFCRPRDDQFGHYACGSEGQKLCLNGWQGVNC
```

Figure 9

Human Delta 1 (GenBank Accession No. AF003522)

MGSRCALALAVLSALLCQVWSSGVFELKLQEFVNKKGLLGNRNCCRGGAGPPPCACRTFFRVCLKHYQASVSPEPPCTYGSAVTPVLGVDSFSLPDGGGA
DSAFSNPIRFPFGFTWPGTFSLIIEALHTDSPDDLATENPERLISRLATQRHLTVGEEWSQDLHSSGRTDLKYSYRFVCDEHYYGEGCSVFCRPRDDAFG
HFTCGERGEKVCNPGWKGPYCTEPICLPGCDEQHGFCDKPGECKCRVGWQGRYCDECIRYPGCLHGTCQQPWQCNCQEGWGGLFCNQDLNYCTHHKPCKN
GATCTNTGQGSYTCSCRPGYTGATCELGIDECDPSPCKNGGSCTDLENSYSCTCPPGFYGKICELSAMTCADGPCFNGGRCSDSPDGGYSCRCPVGYSGF
NCEKKIDYCSSSPCSNGAKCVDLGDAYLCRCQAGFSGRHCDDNVDDCASSPCANGGTCRDGVNDFSCTCPPGYTGRNCSAPVSRCEHAPCHNGATCHERG
HGYVCECARGYGGPNCQFLLPELPPGPAVVDLTEKLEGQGGPFPWVAVCAGVILVLMLLLGCAAVVVCVRLRLQKHRPPADPCRGETETMNNLANCQREK
DISVSIIGATQIKNTNKKADFHGDHSADKNGFKARYPAVDYNLVQDLKGDDTAVRDAHSKRDTKCQPQGSSGEEKGTPTTLRGGEASERKRPDSGCSTSK
DTKYQSVYVISEEKDECVIATEV

Human Delta 3 (GenBank Accession No. NM_016941)

MVSPRMSGLLSQTVILALIFLPQTRPAGVFELQIHSFGPGPGPGAPRSPCSARLPCRLFFRVCLKPGLSEEAAESPCALGAALSARGPVYTEQPGAPAPDL
PLPDGLLQVPFRDAWPGTFSFIIETWREELGDQIGGPAWSLLARVAGRRRLAAGGPWARDIQRAGAWELRFSYRARCEPPAVGTACTRLCRPRSAPSRCGP
GLRPCAPLEDECEAPLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCTVPVSTSSCLSPRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRG
FYGLRCEVSGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGFAGPRCEHDLDDCAGRACANGG
TCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRCYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLLPPALGLLVAAGV
AGAALLLVHVRRRGHSQDAGSRLLAGTPEPSVHALPDALNNLRTQEGSGDGPSSSVDWNRPEDVDPQGIYVISAPSIYAREVATPLFPPLHTGRAGQRQHL
LFPYPSSILSVK

Human Delta 4 (GenBank Accession No. AF 253468)

MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCLKHFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGRN
PLQLPFNFTWPGTFSLIIEAWHAPGDDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCKKRNDHFGHYVCQP
DGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNECIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATCSNS
GQRSYTCTCRPGYTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCRERNQGANYACECPPNFTGSNCEKKVD
RCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCELHVSDCARNPCAHGGTCHDLENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLSTDTFV
CNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREAMNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGLDKSNCG
KQQNHTLDYNLAPGPLGRGTMPGKFPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV

Figure 10

Human Jagged 1 (GenBank Accession No. U73936)

MRSPRTRGRSGRPLSLLLALLCALRAKVCGASGQFELEILSMQNVNGELQNGNCCGGARNPGDRKCTRDECDTYFKVCLKEYQSRVTAGGPCSFGSG
STPVIGGNTFNLKASRGNDRNRIVLPFSFAWPRSYTLLVEAWDSSNDTVQPDSIIEKASHSGMINPSRQWQTLKQNTGVAHFEYQIRVTCDDYYYGF
GCNKFCRPRDDFFGHYACDQNGNKTCMEGWMGPECNRAICRQGCSPKHGSCKLPGDCRCQYGWQGLYCDKCIPHPGCVHGICNEPWQCLCETNWGGQ
LCDKDLNYCGTHQPCLNGGTCSNTGPDKYQCSCPEGYSGPNCEIAEHACLSDPCHNRGSCKETSLGFECECSPGWTGPTCSTNIDDCSPNNCSHGGT
CQDLVNGFKCVCPPQWTGKTCQLDANECEAKPCVNAKSCKNLIASYYCDCLPGWMGQNCDININDCLGQCQNDASCRDLVNGYRCICPPGYAGDHCE
RDIDECASNPCLNGGHCQNEINRFQCLCPTGFSGNLCQLDIDYCEPNPCQNGAQCYNRASDYFCKCPEDYEGKNCSHLKDHCRTTPCEVIDSCTVAM
ASNDTPEGVRYISSNVCGPHGKCKSQSGGKFTCDCNKGFTGTYCHENINDCESNPCRNGGTCIDGVNSYKCICSDGWEGAYCETNINDCSQNPCHNG
GTCRDLVNDFYCDCKNGWKGKTCHSRDSQCDEATCNNGGTCYDEGDAFKCMCPGGWEGTTCNIARNSSCLPNPCHNGGTCVVNGESFTCVCKEGWEG
PICAQNTNDCSPHPCYNSGTCVDGDNWYRCECAPGFAGPDCRININECQSSPCAFGATCVDEINGYRCVCPPGHSGAKCQEVSGRPCITMGSVIPDG
AKWDDDCNTCQCLNGRIACSKVWCGPRPCLLHKGHSECPSGQSCIPILDDQCFVHPCTGVGECRSSSLQPVKTKCTSDSYYQDNCANITFTFNKEMM
SPGLTTEHICSELRNLNILKNVSAEYSIYIACEPSPSANNEIHVAISAEDIRDDGNPIKEITDKIIDLVSKRDGNSSLIAAVAEVRVQRRPLKNRTD
FLVPLLSSVLTVAWICCLVTAFYWCLRKRRKPGSHTHSASEDNTTNNVREQLNQIKNPIEKHGANTVPIKDYENKNSKMSKIRTHNSEVEEDDMDKH
QQKARFAKQPAYTLVDREEKPPNGTPTKHPNWTNKQDNRDLESAQSLNRMEYIV

Human Jagged 2 (GenBank Accession No. AF029778)

MRAQGRGRLPRRLLLLLALWVQAARPMGYFELQLSALRNVNGELLSGACCDGDGRTTRAGGCGHDECDTYVRVCLKEYQAKVTPTGPCSYGHGATPV
LGGNSFYLPPAGAAGDRARARARAGGDQDPGLVVIPFQFAWPRSFTLIVEAWDWDNDTTPNEELLIERVSHAGMINPEDRWKSLHFSGHVAHLELQI
RVRCDENYYSATCNKFCRPRNDFFGHYTCDQYGNKACMDGWMGKECKEAVCKQGCNLLHGGCTVPGECRCSYGWQGRFCDECVPYPGCVHGSCVEPW
QCNCETNWGGLLCDKDLNYCGSHHPCTNGGTCINAEPDQYRCTCPDGYSGRNCEKAEHACTSNPCANGGSCHEVPSGFECHCPSGWSGPTCALDIDE
CASNPCAAGGTCVDQVDGFECICPEQWVGATCQLDANECEGKPCLNAFSCKNLIGGYYCDCIPGWKGINCHINVNDCRGQCQHGGTCKDLVNGYQCV
CPRGFGGRHCELERDKCASSPCHSGGLCEDLADGFHCHCPQGFSGPLCEVDVDLCEPSPCRNGARCYNLEGDYYCACPDDFGGKNCSVPREPCPGGA
CRVIDGCGSDAGPGMPGTAASGVCGPHGRCVSQPGGNFSCICDSGFTGTYCHENIDDCLGQPCRNGGTCIDEVDAFRCFCPSGWEGELCDTNPNDCL
PDPCHSRGRCYDLVNDFYCACDDGWKGKTCHSREFQCDAYTCSNGGTCYDSGDTFRCACPPGWKGSTCAVAKNSSCLPNPCVNGGTCVGSGASFSCI
CRDGWEGRTCTHNTNDCNPLPCYNGGICVDGVNWFRCECAPGFAGPDCRINIDECQSSPCAYGATCVDEINGYRCSCPPGRAGPRCQEVIGFGRSCW
SRGTPFPHGSSWVEDCNSCRCLDGRRDCSKVWCGWKPCLLAGQPEALSAQCPLGQRCLEKAPGQCLRPPCEAWGECGAEEPPSTPCLPRSGHLDNNC
ARLTLHFNRDHVPQGTTVGAICSGIRSLPATRAVARDRLLVLLCDRASSGASAVEVAVSFSPARDLPDSSLIQGAAHAIVAAITQRGNSSLLLAVTE
VKVETVVTGGSSTGLLVPVLCGAFSVLWLACVVLCVWWTRKRRKERERSRLPREESANNQWAPLNPIRNPIERPGGHKDVLYQCKNFTPPPRRADEA
LPGPAGHAAVREDEEDEDLGRGEEDSLEAEKFLSHKFTKDPGRSPGRPAHWASGPKVDNRAVRSINEARYAGKE

Figure 11